REMARKS

Claims 1-13, 15, 33 and 43-45 are pending in the application. By this Amendment, Applicants have amended claims 1, 44, and 45. Support for the amendments can be found in the specification and claims as originally filed. The present Amendment does not introduce any new matter and thus, its entry is requested. Upon entry of the present Amendment, claims 1-13, 15, 33, and 43-45, as amended, will be pending and under examination.

The November 4, 2005 Office Action

Examiner's Claim Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-13, 15, 33 and 43-45 under 35 U.S.C. 112, second paragraph, as being indefinite. The Examiner stated that claim 1 is indefinite because of the newly added limitation of the A variable having at least 19 carbon atoms. According to the Examiner, this limitation is in conflict with the limitations, "**12** $\leq$ p+q $\leq$ 30" and "p+q representing 12, 13 or 14" and the proviso "when p+q is 12 or 14." The Examiner pointed out that the total number of carbon atoms in the A radical would be less than 19 in each of these instances. The Examiner also directed attention to claims 15, 44, and 45, raising the same concern.

In response, Applicants have amended claims 1, 44, and 45 by having them recite that ***15***$\leq$ p+q $\leq$ 30, and by deleting provisos that relate to p+q being 12 or 14, or are otherwise inconsistent with the amended claim language. Applicants believe that these claim amendments fully overcome the Examiner's concerns. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-13, 15, 33 and 43-45 under 35 U.S.C. 112, second paragraph.

Examiner's Claim Rejections Under 35 U.S.C. §103

The Examiner rejected claims 1-13, 15, 33, and 43-45 under 35 U.S.C. §103(a) as allegedly being unpatentable over AT 393505 and Eibl, et al. (EP 534,445), each taken alone, for reasons already of record. Specifically, the Examiner has continued to take the position that the cited references teach phosphates, phosphoamines, and phosphate esters which are structurally

similar to the instant claimed compounds, asserting that the difference between some of the compounds of the prior art and the claimed compounds "is that the instant claimed compounds are generically described in the prior art." In particular, the Examiner again directed attention to pages 3, 4, 17, and 22-25 and Examples 13 and 14 of AT 393505. According to the Examiner, this reference also teaches phosphate esters which are structurally similar to the instant compounds, the specific example compounds differing from Applicants' claimed compounds only by a methylene group. The Examiner concluded that Applicants' claimed invention would therefore have been obvious to one of ordinary skill in the art.

The Examiner also stated that Applicants' arguments filed August 5, 2005 have been fully considered. According to the Examiner, Applicants argued that the instant claimed compounds have improved antitumor activity when the double bound in variable A is at a distance from the O (oxygen linkage in variable A) which does not appear in a naturally-occurring corresponding radical and A is a radical having at least 19 carbon atoms. The Examiner stated that Applicants also argued that the instant claimed compounds exhibit further surprising advantages over the cited prior art compounds in that although the prior art compounds show good anti-tumor activity, the prior art compounds exhibit significant toxicity and therefore such compounds having a short carbon chain cannot be administered intravenously but only orally where toxicity is not a problem.

The Examiner noted that Applicants further argued that, in contrast to the teachings in the art, it has been surprisingly found that the toxicity problems known in the art no longer occur with compounds having a double bond in a non-naturally occurring position, as claimed in the present invention and that the tumor-effective concentrations of these compounds are no longer toxic. The Examiner stated that Applicants argued that this is demonstrated in the tests concerning (Z)-10-docosenyl-l-phosphocholine submitted with Applicants' December 15, 2004 response.

The Examiner indicated that all of Applicants' arguments have been considered but have not been found persuasive. According to the Examiner, Applicants claim phosphates and phosphoamines. The Examiner asserted that AT 393505 teaches phosphates and phosphoamines that are structurally similar to the instant claimed compounds, and that can be administered topically, orally or intravenously. The Examiner stated that Eibl et al. also teach phosphate

esters, which are structurally similar to the instant claimed compounds, that can be administered topically or orally. According to the Examiner, Applicants have not provided the Office with factual persuasive evidence that is demonstrated in a persuasive side-by-side showing of unexpected, beneficial, and superior results of the instant claimed compounds, under examination, over the specie prepared in the cited prior art. The Examiner asserted that Attorney arguments asserting unexpected results cannot take the place of evidence in the record, and cited In re DeBlauwe, 222 U.S.P.Q. 191, 196 (Fed. Cir. 1984). The Examiner asserted that an Applicant relying upon a comparative showing to rebut a prima facie case must compare his claimed invention with the closest prior art. In re Holladay, 199 USPQ 516, 1978.

In response, Applicants respectfully traverse the Examiner's rejection. Applicants reiterate that the claims recite that "A is a radical having at least 19 carbon atoms." Thus, in the claimed compounds, the double bond in A is at a distance from O which does not appear in a naturally-occurring corresponding radical, (i.e., the double bond is not at the same position as it would be in the underlying naturally-occurring alcohol or acid) *and* A is a radical having at least 19 carbon atoms. As set forth throughout the specification, such modifications, achieved through a novel process, allow one to change and specifically control the physical, biochemical, and biological properties of the compounds. Such structural variations in the apolar region lead to compounds exhibiting improved antitumor activity (See page 4, lines 15-24 and page 14, lines 20-32), and further allow one to produce the compounds in industrial quantities.

Applicants additionally reiterate that the compounds of the present invention, as reflected in the amended claims, exhibit further surprising advantages over the prior art compounds. In that regard, Applicants note that shorter-chained compounds, i.e., those having a chain length up to 18 carbon atoms, such as those in Examples 13 and 14 of AT 393505 (relied on by the Examiner in rejecting the claims), show good anti-tumor activity but exhibit significant toxicity, such as hemolysis and thrombophlebitis. Therefore, such compounds having a short carbon chain (including, in particular, those having a chain of 16 or 18 carbons) cannot be administered intravenously, but rather only orally, where the toxicity is not a problem. In contrast, prior known compounds having greater chain length, i.e., having at least 19 carbon atoms, did not exhibit anti-tumor effect when administered orally because they could not be taken up in sufficient amounts by that route. These compounds thus could only be administered in effective

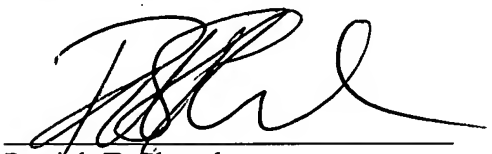
amounts intravenously. However, such administration was not appropriate due to the toxicity problems noted above. With the present invention, however, as noted previously, it has been surprisingly found that the toxicity problems known in the art no longer occur with compounds having a double bond in a non-naturally occurring position, as claimed in the present invention. Moreover, it was surprisingly found that tumor-effective concentrations of these compounds are no-longer toxic. As previously pointed out, this was also demonstrated in the tests concerning (Z)-10-docosenyl-1-phosphocholine submitted with Applicants' December 15, 2004 response. Thus, the compounds of the present invention, which include a double bond in a non-naturally occurring position and a chain length of at least 19 carbon atoms, exhibit surprising and unexpected properties over the prior art compounds, including, *inter alia*, the suitability for intravenous administration due to their retained effectiveness and low toxicity. Thus the claimed compounds represent surprisingly useful agents.

Applicants also note the Examiner's requirement that results obtained in a side-by-side comparison of the claimed compound with the closest prior art, (i.e., hexadecenylphosphocholine) be presented if Applicants are to rely on the invention's unexpected or surprising properties. Applicants point out to the Examiner that it is impractical to present the side-by-side comparison that the Examiner is seeking, given what is a difficult and complicated procedure to prepare hexadecenylphosphocholine. The tests submitted thus are sufficient to show nonobviousness of the claimed invention, as they demonstrate that the compounds of the present invention are more effective than the conventional related agent, hexadecylphosphocholine. Applicants direct attention to MPEP §716.02(e), suggesting that inconsequential deviations from such comparisons are permissible if an explanation (such as that presented here), is provided. Accordingly, Applicants' invention is not rendered obvious over the art cited by the Examiner. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-13, 15, 33, and 43-45 under 35 U.S.C. §103(a).

In view of the above remarks and claim amendments, Applicants believe that the Examiner's rejections set forth in the November 4, 2005 Office Action have been fully overcome and that the present claims fully satisfy the patent statutes. Applicants therefore believe that the application is in condition for allowance. The Examiner is invited to telephone

the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,



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